

# Jaundice and Kernicterus in the Newborn

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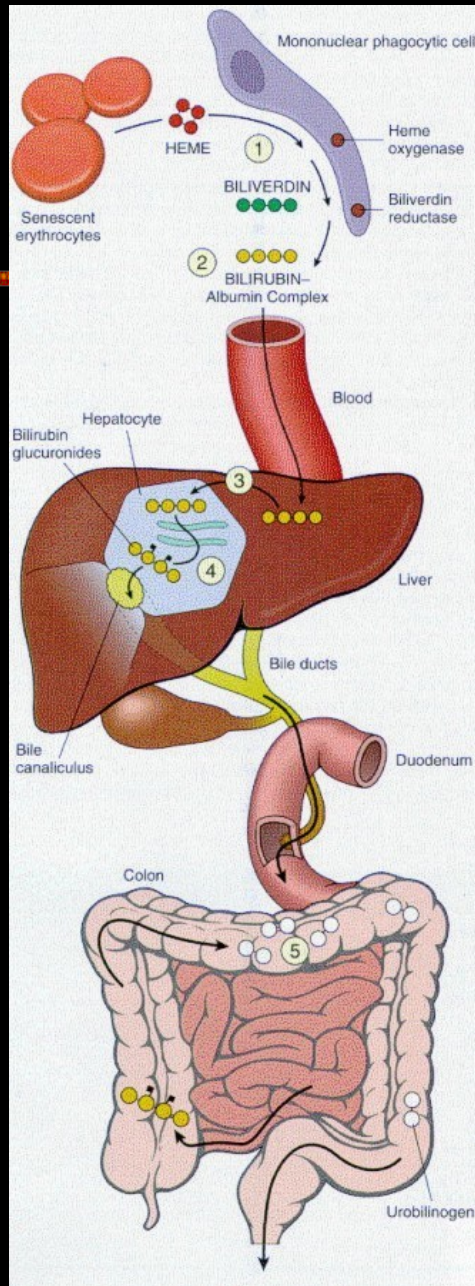
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# Introduction

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- Neonatal jaundice affects 60% of term babies and 80% of pre-term babies in the first 3 days of life
  - Accounts for 75% of hospital readmissions in the first week after birth
  - Shortened newborn hospital stays has increased readmission rates up to 3-fold
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- Rapid breakdown of erythrocytes (life span only 90 days instead of 120 days) accounts for 75% of bilirubin production
- Newborn liver is deficient (about 0.1 to 1% of adult) in enzyme activity (uridine diphosphate glucuronyl transferase) for bilirubin metabolism
- Newborns have higher levels of intestinal *Beta*-glucuronidase, resulting in greater resorption of bilirubin through the enterohepatic circulation (this is especially true of breastfed babies, who



# Introduction

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- Jaundice in healthy, term infants is called “physiologic” because it occurs universally
  - Bilirubin levels peak at 5 to 12 mg/dL on the 2nd or 3rd day of life
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# Introduction

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- Jaundice should be considered nonphysiologic if:
    - It occurs at less than 24 hours of life
    - Bilirubin rises faster than 0.5 mg/dL per hour or faster than 5 mg/dL per day
    - Total bilirubin exceeds 15 mg/dL in a term baby or 10 mg/dL in a pre-term baby
    - Evidence of hemolysis exists
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# Introduction

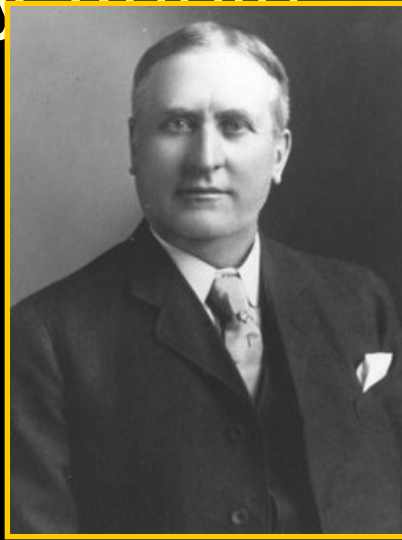
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- Elevated bilirubin normally does not persist beyond 10 days in a full-term infant or 21 days in a pre-term infant
  - However, breast-fed babies may have prolonged jaundice
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# History

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- Jaundice was discovered by Dr. William Rubin, who, of course, coined the term “Billy Rubin”



Dr. William Rubin\*

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\*Lighten up! This is a joke. The picture above is actually Mr. J. J. Brown, the husband of Molly Brown



# History (for real, this time)

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- Recognized for many centuries, scientific investigation of newborn jaundice began in the last half of the 18<sup>th</sup> century
  - In 1785 Jean Babtiste Thimotee Baumes described the clinical course of 10 infants to the University of Paris
  - Often considered the first “scientific” treatise on newborn jaundice
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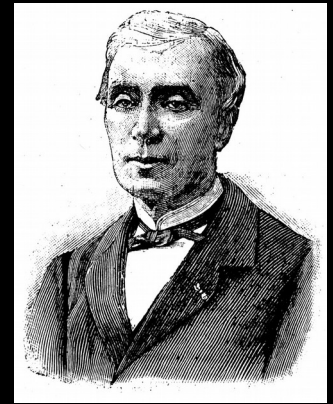
# History

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- During the first half of the 19th century, several doctoral theses at the University of Paris were on neonatal jaundice
  - These theses were long on opinion and speculation, short on science
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# History

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- Jaques Franscois Edouard Hervieux defended his thesis *On the Jaundice of Newborns* in 1847 to the University of Paris
  - Provided sharp criticism of the preceding theses
  - Reported on 45 cases, 44 of which had died and undergone autopsy by him
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### **Summary of Hervieux's Clinical and Epidemiological Observations on Neonatal Jaundice**

1. The cause of neonatal jaundice is not known, but one can state that jaundice in the neonate is a manifestation of a recently established function that for a limited time exceeds its physiological limits.
2. Neonatal jaundice is a physiological condition.
3. Neonatal jaundice is, by itself, never fatal
4. Neonatal jaundice appears during the first 2 to 4 days of life and lasts for 1 to 2 weeks. It never reappears in the following months.
5. There is a cephalocaudal progression in the appearance of jaundice - the extremities are always last to be affected. When jaundice disappears, the order is reversed.
6. Neonatal jaundice is very common - approximately two thirds of all infants are affected. The prognosis in the absence of complicating conditions is benign.
7. Jaundice is not seen in foundlings who are wet-nursed, or in infants nursed by a woman who gave birth a long time ago.
8. The most frequent complicating conditions are scleredema, diarrhea, and thrush.
9. Treatment consists of combating the complicating conditions. Isolated neonatal jaundice does not need treatment.
10. In neonatal jaundice, the yellow color is found throughout the tissues of the body, including the brain.

# History

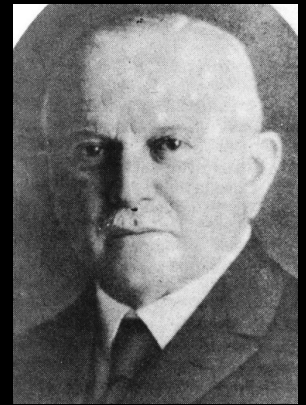
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- Johannes Orth published the first anatomical pictures of kernicterus (c. 1875)
  - Described the jaundiced brain of a 2-day old who had become extremely jaundiced shortly after birth
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# History

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- Christian Georg Schmorl coined the term *kernicterus* (“jaundice of the nuclei”)
  - In 1904, he published findings of 280 neonatal autopsies, 120 of whom were jaundiced at death
  - The majority (114/120) of those jaundiced babies had kernicterus
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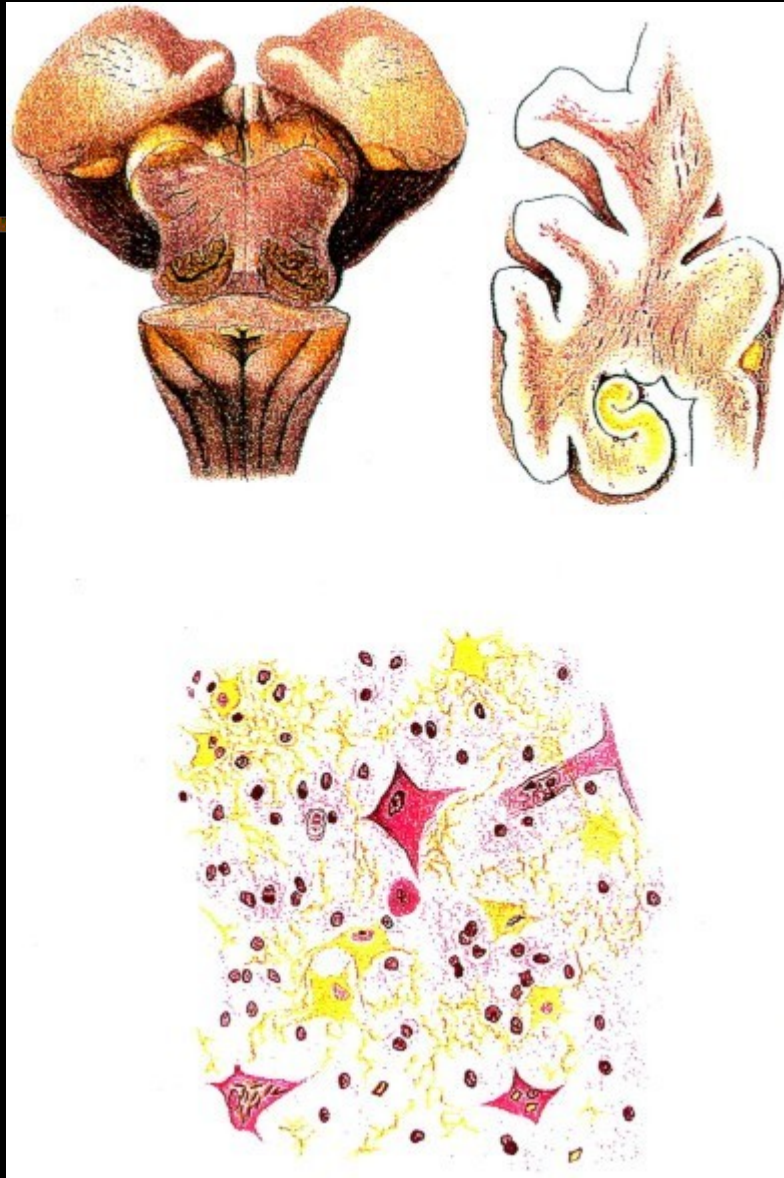
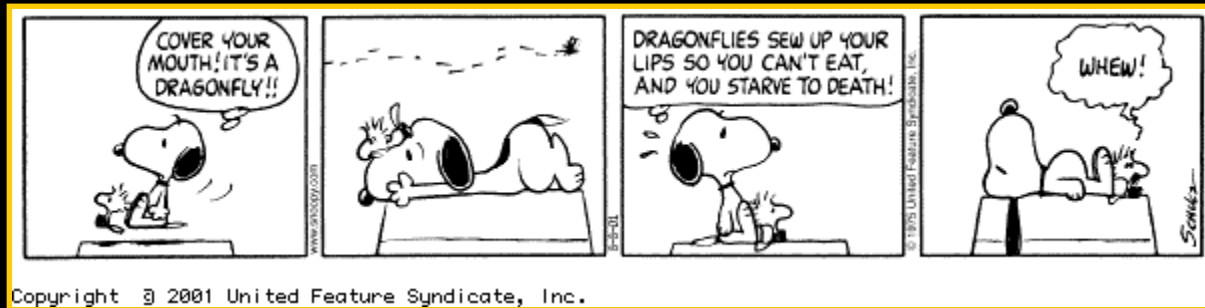


Figure from  
Schmorl's 1904  
publication,  
illustrating  
kernicterus

# Debunking Urban Legends





# Debunking Urban Legends

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*Don't swallow a dragonfly.*

“Dragonflies sew up your lips so you can't eat and you starve to death!”

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# Debunking Urban Legends



# Debunking Urban Legends



# Debunking Urban Legends

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- “Kernicterus is exclusively a disease of sick, premature babies and/or babies with hemolytic disease”
  - “Kernicterus does not occur in healthy, term babies with no hemolysis”
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# Case Histories - Kernicterus

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- Healthy term babies with kernicterus reported in *Morbidity and Mortality Weekly Report*, June 15, 2001
  - <http://www.cdc.gov/mmwr/>
  - Cases reported occurred between 1994-1998
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# Cases from MMWR

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**Case 1.** In 1994, an apparently healthy white boy was born at 37 weeks' gestation weighing 6 lbs, 13 oz (3090 g). Delivery was uncomplicated. His 1 minute and 5 minute Apgar scores were eight and nine, respectively (normal range: seven--10). His mother's blood type was O+, and the newborn was A+, Coombs negative. On discharge at 20 hours, he was alert and nursing well; a 2-week follow-up appointment was scheduled at a pediatric clinic. On day 9, the infant was taken to a pediatric clinic with jaundice. The condition was thought to be the result of breastfeeding. That evening, he exhibited lethargy, was not nursing, and had "pumpkin orange" skin coloration. On day 10, the parents notified their physician about the infant's lethargy and poor eating and were given an appointment for the following morning. During a pediatric appointment on day 11, the infant weighed 5 lbs, 10 oz (2552 g), was dehydrated, and jaundiced. A tested serum sample revealed an elevated bilirubin of 41.5 mg/dL (normal range at age >72 hours: <17 mg/dL). Despite treatment with phototherapy and two double-volume exchange transfusions, on day 11, he developed athetosis, oral-motor dysfunction requiring a gastrostomy tube, and dental dysplasia. Kernicterus was diagnosed at age 6 months.

# Cases from MMWR

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**Case 2.** In 1995, an apparently healthy white boy was born at 37 weeks' gestation weighing 6 lbs, 5 oz (2863 g). Apgar scores were eight and nine at 1 and 5 minutes, respectively. At 17, 23, and 33 hours, jaundice was noted. No serum bilirubin level or ABO or Rh status was disclosed. Examination revealed normal neurologic and physical findings, and he was discharged after 36 hours; a follow-up appointment at a pediatric clinic was scheduled at 1 week. On day 4, the patient exhibited lethargy and poor breastfeeding. On day 5, he was admitted to a hospital. Laboratory findings included a bilirubin level of 34.6 mg/dL, and phototherapy was started. Later that day, the patient developed opisthotonus, a high-pitched cry, and poor suckling and later developed athetoid cerebral palsy, hearing loss, and gaze paresis. Kernicterus was diagnosed at age 18 months.

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# Cases from MMWR

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**Case 3.** In 1997, an apparently healthy white boy was born at 37 weeks' gestation weighing 8 lbs, 2 oz (3686 g). His Apgar scores were nine at 1 and 5 minutes. On discharge at 22 hours, a cephalohematoma and heart murmur were noted. The following day, the infant was taken to a pediatric clinic where examination found jaundice but no heart murmur. Fifteen minutes of sunlight per day was recommended as treatment. During the next 4 days, the infant developed lethargy and poor breastfeeding. On day 6, he was taken to a pediatric clinic where a serum sample was drawn and tested. Results included a bilirubin level of 27 mg/dL; phototherapy was started. By 11 p.m., the patient's bilirubin peaked at 33.4 mg/dL, and he received an exchange transfusion. During the next 4 months, he developed athetoid cerebral palsy, oral-motor dysfunction requiring a gastrostomy tube, and gaze paresis. Kernicterus was diagnosed at age 4 months.

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# Cases from MMWR

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**Case 4.** In 1998, an apparently healthy white boy was born at 39 weeks' gestation weighing 9 lbs, 8 oz (4313 g). Pregnancy was unremarkable but delivery required vacuum extraction. His Apgar scores were eight and nine at 1 and 5 minutes, respectively. AO blood incompatibility was noted and Rh status was unknown. At 22 hours, he appeared jaundiced; at 52 hours, he was discharged with the treatment recommendation that he receive sunlight. The infant was alert and nursed well during the next 11 days. However, at his follow-up examination on day 12, he appeared jaundiced. The initial serum bilirubin level was 23.6 mg/dL, which peaked at 29.4 mg/dL. The same day, the infant was admitted to a hospital for phototherapy. During the next 4 months, he developed athetoid cerebral palsy, hearing loss, and enamel hypoplasia, and kernicterus was diagnosed at age 4 months.

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# How did we get here?

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- Urban legends - a widespread belief (without scientific basis) that term babies without hemolytic disease were safe from kernicterus
  - A “kinder, gentler approach” advocated in the literature (Maisels, 1992)
  - Adoption of looser treatment standards by the AAP (1994)
    - <http://www.aap.org/policy/hyperb.htm>
  - Aggressive early postnatal discharge policies
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# Kernicterus

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- Kernicterus may result from severe hyperbilirubinemia
  - Characterized by staining of the basal ganglia and diffuse neuronal damage with severe neurologic sequelae
  - Rarely occurs with bilirubin levels under 20 mg/dl
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# Kernicterus

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- Kernicterus is a very real danger when bilirubin levels approach or exceed 30 mg/dl
  - Risk factors include prematurity and hemolytic disease
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# Bilirubin encephalopathy

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- Three phases:
    - Lethargy, hypotonia, weak suck (first 2 to 3 days)
    - Progressive hypotonia, opisthotonus, fever, seizures, high-pitched cry
    - Prolonged hypotonia (several years) progressing to hypertonia
  - End stage: developmental and motor delays, chorioathetoid cerebral palsy
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# Jaundice

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- Risk factors:

- Breast-feeding

- In one study, breastfeeding increased risk of jaundice 3-fold

- Low birth weight / prematurity

- Ethnicity

- East Asian, Native American
      - G6PD deficiency more common in Mediterraneans
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# Jaundice

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- Risk factors

- Hemolysis

- Coombs positive Rh or ABO setup
    - Bruising or cephalhmatoma

- Poor feeding

- Early onset of jaundice

- History of a sibling with jaundice

- Infection

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## **JAUNDICE Acronym Summarizes Major Risk Factors for Hyperbilirubinemia in Full-Term Newborns**

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- **J**aundice within first 24 hours after birth.
  - **A** sibling who was jaundiced as a neonate.
  - **U**nrecognized hemolysis such as ABO blood type incompatibility or Rh incompatibility.
  - **N**onoptimal sucking/nursing.
  - **D**eficiency in glucose-6-phosphate dehydrogenase, a genetic disorder.
  - **I**nfection.
  - **C**ephalohematomas/bruising.
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# Diagnosis

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- Jaundice is visible when bilirubin exceeds 5 mg/dL
  - Visual estimates of total serum bilirubin are unreliable
  - Laboratory evaluation is normally needed for “nonphysiologic” jaundice (i.e. rapid onset of jaundice, evidence of hemolysis, etc.)
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# Diagnosis

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- Blood type and Coombs should be done to check for Rh or ABO hemolytic potential
  - With suspected hemolysis, additional lab (hematocrit, reticulocyte count, peripheral smear) may be useful
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# Diagnosis

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- Hemolysis due to G6PD deficiency, piruvate kinase deficiency, hereditary spherocytosis, etc., may require more specialized investigation
  - Direct (conjugated) bilirubin should be done at least once, to rule-out biliary atresia, congenital infection (TORCH), hepatitis, galactosemia, etc.
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# Diagnosis

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- Late onset or prolonged jaundice might suggest Crigler-Najjar (glucuronyl transferase deficiency)
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# Treatment

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- American Academy of Pediatrics practice parameter for treatment of jaundice in the healthy, full-term newborn was developed and published in 1994
    - <http://www.aap.org/policy/hyperb.htm>
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## Management of Hyperbilirubinemia in the Healthy Term Newborn\*

Age, hours	TSB Level, mg/dL (pmol/L)			
	Consider Phototherapy†	Phototherapy	Exchange Transfusion if Intensive Phototherapy Fails‡	Exchange Transfusion and Intensive Phototherapy
≤24§	...	...	...	...
25-48	≥12 (170)	≥15 (260)	≥20 (340)	≥25 (430)
49-72	≥15 (260)	≥18 (310)	≥25 (430)	≥30 (510)
>72	≥17 (290)	≥20 (340)	≥25 (430)	≥30 (510)

\* TSB indicates total serum bilirubin.

† Phototherapy at these TSB levels is a clinical option, meaning that the intervention is available and may be used on the basis of individual clinical judgment.

‡ Intensive phototherapy should produce a decline of TSB of 1 to 2 mg/dL within 4 to 6 hours and the TSB level should continue to fall and remain below the threshold level for exchange transfusion. If this does not occur, it is considered a failure of phototherapy.

§ Term infants who are clinically jaundiced at ≤24 hours old are not considered healthy and require further evaluation.

# Treatment

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- Phototherapy is the mainstay of treatment
  - If needed, can intensify therapy by using double-bank and/or fiberoptic blanket
  - Should be able to achieve a drop of 1 to 2 mg/dL in the first 4 to 6 hours
  - Light emissions at 425 to 475 nm convert bilirubin to a water-soluble form that can be excreted in bile or urine
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# Treatment

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- Home phototherapy has been shown to be safe and effective *in situations where intense phototherapy is not required*
  - Lower cost, better maintenance of breastfeeding
  - Constant and proper use of the phototherapy blanket must be emphasized
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# Treatment

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- Side-effects of phototherapy include diarrhea, dehydration, rash, and bronze discoloration of the skin
  - Breastfeeding should be increased to every 2 to 2 ½ hours, and supplemental formula can be considered if lactation is insufficient
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# Treatment

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- Exchange transfusion is rarely necessary if phototherapy is initiated in a timely manner
  - Should be considered for bilirubin over 25 mg/dL if phototherapy does not quickly lower level
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# Treatment

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- Exchange transfusion carries significantly greater risk than phototherapy
  - Risk of major morbidity is ~5%, and the risk of death is 2 to 3 per 1,000
  - Increases risk of infection, necrotizing enterocolitis, acidosis, hypocalcemia, hypoglycemia, electrolyte imbalance, and air embolism
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# Prevention

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- To minimize risks of perinatal jaundice, parent education and monitoring are necessary
  - Newborns discharged from the hospital before 48 hours of age must receive follow-up care within 72 hours
    - Low-risk may have a home-health nurse visit
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# Summary

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- Neonatal jaundice is the most common reason for hospital readmission in the first two weeks of life
- Kernicterus is uncommon, but on the rise
- Kernicterus is a preventable complication of neonatal jaundice
  - Identification of infants at-risk
  - Education of parents
  - Vigilant monitoring and follow-up

# Comments or Questions?

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